

sample derived from a cell, a tissue or an organism which has been exposed to a sample containing an endocrine disruptor, a gene of which the signal intensity is significantly different among the two nucleic acid samples can be detected. Specifically, an array is subjected to hybridization with a nucleic acid sample labeled as described above. A signal intensity of radioactivity, fluorescence, luminescence or the like for the hybridized array is detected using a specialized measuring instrument such as a chromatogram scanner or image analyzer. A gene of which the expression is significantly altered as a result of the influence of an endocrine disruptor can be detected based on the difference in the signal intensity.

The gene expression for a control nucleic acid sample can be compared on the same DNA array with that for a nucleic acid sample derived from a cell, a tissue or an organism that has been exposed to an endocrine disruptor on the same DNA array by using a multiple wavelength detecting fluorescence analyzer which is capable of detecting plural labels (e.g., two types of fluorescence). For example, a nucleic acid sample derived from a cell which has been exposed to an endocrine disruptor is fluorescence-labeled with Cy3-dUTP, whereas a control nucleic acid sample is fluorescence-labeled with Cy5-dUTP. The difference in gene expression between the two nucleic acid samples can be

detected as difference in color by mixing equal amounts of the nucleic acid samples and subjecting the mixture to hybridization with a DNA array. A gene of which the expression level is significantly altered as a result of the influence of the endocrine disruptor can be detected based on the results.

The gene is also useful as an index for detecting an endocrine disruptor.

A gene that is influenced by an endocrine disruptor is selected by comparing a signal intensity detected as an index of expression level with that obtained using a nucleic acid sample prepared using a control sample. For example, a value is calculated by dividing a fluorescence signal value for a sample containing an endocrine disruptor by a fluorescence signal value for a control sample. A value greater than 1.00 indicates that the gene expression is promoted by the treatment with the test substance. A value smaller than 1.00 indicates that the gene expression is suppressed by the treatment with the test substance. A value equal to 1.00 indicates that the gene is not influenced by the treatment with the test substance. If the expression is promoted, the value is greater than 1.10, preferably 1.30, more preferably 2.00. If the expression is suppressed, the value is smaller than 0.90, preferably 0.80, more preferably 0.70.

As described above, the expression of genes that are influenced by endocrine disruptors (for example, a gene for a nuclear receptor in a cell and a number of genes involved in the downstream signal transduction pathway) can be detected simultaneously, in vitro, rapidly and with high sensitivity according to the method of the present invention. In addition, it is possible to find involvement of a known gene in a previously unknown signal transduction pathway.

(2) An endocrine disruptor can be detected using the expression of a gene that is influenced by the endocrine disruptor as an index as follows.

A DNA array, onto which a gene which has been confirmed to be influenced by an endocrine disruptor is immobilized as described above, is prepared.

A nucleic acid sample is prepared from a cell, a tissue or an organism which is suspected to be influenced by the endocrine disruptor as described above. The nucleic acid sample is then hybridized as described above. Change in gene expression can be determined based on the difference between the signal intensities. The presence of the endocrine disruptor can be determined based on the results.

In another embodiment, the presence of an endocrine disruptor can be also determined as follows. An